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SAFETY ASSESSMENT

SEND Frequently Asked Questions & Resources

The Standard Exchange of Nonclinical Data (SEND) is an implementation of the CDISC Study Data Tabulation Model (SDTM) that provides a framework for the standardized, electronic representation of individual animal study data. As a biotech and pharmaceutical company, you are ultimately responsible for the inclusion of SEND datasets as part of regulatory submissions. Your submission-ready SEND packages will need to include all necessary accompanying materials (define.xml, nsdrg, and dataset validation reports) for your study.

Connect with a SEND Expert

The Charles River SEND Experts have been active members of CDISC and PhUSE teams since the inception of SEND guidelines.

SEND Resources

- CDISC SEND
- Study Data Technical Conformance Guide and Data Standards Catalog
- Electronic Common Technical Document (eCTD) and Technical Rejection Criteria
- FDA Study Data Standards Resources
- PhUSE Implementation Wiki

Frequently Asked Questions By Topic

Gene Therapy

Can you give an update on SEND requirements for gene therapy studies? What do CDER and CBER require?

SEND is required for single dose toxicity, repeat-dose toxicity, carcinogenicity, safety pharmacology cardiovascular and respiratory studies for submissions to CDER. CBER does not require SEND.

SEND Guidelines

How will SEND v3.1.1 be implemented? Will the FDA issue an FR notice with dates?

Typically, when the FDA is ready to accept a standard, that version of the standard will be added to the FDA Data Standards Catalog with support dates. An FR notice is generally not needed in order to add a standard to the catalog; however, one can be issued.

We've heard the FDA is giving a 30-day grace period for the filing of SEND datasets with a submission requiring datasets; can you confirm this?

We have not heard of any grace period, and this information conflicts with other information we have received from FDA. We suggest that you contact eDATA to get an official response from FDA on this subject.

Which define file should you submit to the FDA if there are multiple define files?

Define 1.0 the following files must be submitted: define.xml, define1-0-0.xsl, define.css, define.pdf

Define 2.0 mandated on and after March 15, 2019, the following files must be submitted: define.xml, define2-0-0.xsl, define.css.

If I have a Word and PDF version in the SEND package, should I remove the Word version from the package before submitting to the FDA?

Yes. Only the PDF version of the nSDRG should be included in the submission.

Once SEND datasets are finalized and sent to my company, are there any additional steps needed for electronic publishing and submission to FDA?

Charles River provides a submission-ready SEND dataset package. You will just need to incorporate those files into your eCTD structure to submit.

Do you provide a study data reviewer guide for each study that requires SEND datasets?

A Nonclinical Study Data Reviewer's Guide (nSDRG) will be provided with each SEND package.

If we get a SEND dataset from our CRO, are there any free programs available to open and review the dataset?

You can use the SAS Universal Viewer to view SEND datasets.

How do you populate the MICHRON and MIDISTR variable with 3.1?

MICHRON and MIDISTR are populated according to the controlled terminology for these variables.

If a study examines special biomarkers related to mechanism of action, are these to be included in the SEND package?

Standard biomarkers are in-scope for SEND and will be included. If there are special biomarkers that are not within-scope it will be mentioned in the nSDRG.

Is it standard that SEND will be required on studies and that PIs will need to provide their domains? Do you handle this or is it a Sponsor's responsibility to discuss SEND with each study contributor?

The Sponsor should ensure that each third party can provide SEND domains for their portion of the study or arrange for SEND conversion for those data. Charles River will create a single integrated SEND dataset.

Would you choose SEND or INHAND to do data mining within toxicologic pathology data?

The choice between SEND and INHAND should be made based on the needs of your organization.

Should *in vivo* drug-drug interaction studies be SEND-compliant?

SEND is required for single dose toxicity, repeat-dose toxicity and carcinogenicity studies if the study protocol was signed on or after December 17, 2016. SEND is also required for cardiovascular and respiratory studies if the study protocol was signed on or after March 15, 2019.

Is the SEND database applicable for a local tolerance study that involves repeated dose administration for 14 days?

Yes. If this study protocol was signed on or after December 17, 2016 and this study will be submitted in eCTD section 4.2.3.2 Repeat-Dose Toxicity. If the study is a local tolerance study as defined (a toxicology study that assesses the effects of a substance when administered to a restricted portion of the body) in the eCTD structure 4.2.3.6, these studies should be filed in the local tolerance section 4.2.3.6 of the eCTD structure and do not require SEND.

Is SEND also in effect for animal rule studies?

SEND is required for animal rule studies (see SENDIG-AR-v1.0). SENDIG-AR-v1.0 will be required for studies starting on or after March 15, 2022 (protocol signature date). Please see the Data Standards Catalog on the FDA's Study Data Standards Resource page.

Investigational New Drug & Complete Programs

If a draft report is submitted with the IND, can the SEND files be submitted subsequently with the final report?

If the draft report is submitted, SEND datasets based on the draft report must also be submitted. SEND datasets based on the final report will be submitted with the final report. Think of the report and SEND dataset as a pair: for each version of the report submitted, you must submit a SEND dataset.

If the SEND version changes between the time a study is submitted to an IND and the date the NDA is filed, do the SEND datasets for the early studies have to be revised to the newer version?

No changes will be required to your existing SEND package. The required SEND version is determined by the date the Study Director signs the study protocol.

Is SEND required for IND if a cardiovascular telemetry study is done prior to March 15, 2021?

If the study protocol for a CV telemetry study is signed by the Study Director on or after March 15, 2019, SEND datasets are not required for the IND. They are, however, required for the NDA, and SEND should be included within the contract for this study.

What is the requirement for interim reports that are used to support an IND?

If an interim report is submitted, then an associated SEND package should also be submitted.

For an ANDA submission to conduct repeat-dose toxicity studies for an impurity qualification, is SEND required?

SEND is required for single-dose toxicity, repeat-dose toxicity, and carcinogenicity studies for ANDA submissions if the study protocol was signed on or after December 17, 2016.

Cardiovascular, Respiratory, & Central Nervous System

For safety respiratory and cardiovascular studies that were initiated prior to the implementation date, is the simplified ts.xpt file required? Is it required for all future IND submissions?

No. The TRC does not require a simplified ts.xpt file for studies in the safety pharmacology (4.2.1.3) folder of the eCTD now; however, Charles River can supply one if needed.

For SEND 3.1 and cardiovascular and respiratory studies, does the guidance include *in vitro* hERG studies, or just *in vivo* cardiovascular studies?

Only cardiovascular and respiratory studies are in-scope for SENDIG v3.1. All *in vitro* and CNS studies are out of scope.

When will CNS safety pharmacology studies need SEND datasets?

There is no date planned for CNS studies.

If respiratory or cardiovascular endpoints are incorporated in repeat-dose toxicology studies, would just the repeat-dose tox SEND file cover the safety pharmacology endpoints incorporated in the tox study?

The SEND v3.1 dataset for the repeat-dose tox study will include the applicable safety pharmacology domains (CV and RE).

What is the difference between 3.0 and 3.1? Is it just the addition of CV and RE safety pharmacology studies or it is much more?

The differences between SENDIG v3.0 and SENDIG v3.1 include more than just the addition of CV and RE for safety pharmacology studies. Changes include additional variables in several domains, and some fixes. Please see the SENDIG 3.1 Appendix D: Revision History for a complete list of changes.

GLP Studies

If we have done an exploratory non-GLP study of limited scope to just look at the reversibility of one organ effect, would this still require SEND datasets, since it's not a full toxicology study and done only to support a previous study?

This depends on the scope and content of the study. If you are unsure, you should contact the FDA eDATA for an official answer.

On a GLP study, if there are non-GLP data collected (e.g., BioA data generated by sponsor), how should this be handled? Does PK data need to be included?

The GLP status does not affect SEND requirements. SEND is required for GLP and non-GLP studies that have individual animal data listings, as SEND is the electronic representation of those individual animal listings. Pharmacokinetic Concentrations data are included within the PC domain, and Pharmacokinetic Parameters data are included within the PP domain in the SEND dataset.

Will the non-GLP investigative portions of a GLP repeat-dose study have to be included in SEND format?

All in-scope data should be included in SEND, regardless of GLP status.

What are the GLP requirements for SEND datasets?

SEND datasets are not subject to FDA Part 58. The systems to create the SEND dataset are typically subject to validation per FDA 21 CFR Part 11.

Will SEND be required for local tolerance studies (e.g., skin irritation, skin sensitization) at some point? Do you know when they will be implemented?

Yes. These data will be modelled in SEND; however, no implementation timing is currently available.

What histopathology data is part of SEND? Do you use abbreviations?

If you collect finding and severity, both the finding and severity need to be included in the SEND dataset. Abbreviations are not typically used in the MI domain. SEND datasets are generated using controlled terminology as required by the SENDIG.

How is bioanalytical and toxicokinetic data (TK parameters) provided as part of SEND, especially if Sponsors are collecting it themselves? How is it integrated with the in-life study?

A Sponsor or Sponsor's third parties conducting any part of the study are expected to provide fully-compliant SEND datasets for the relevant domains (including any comments, RELRECs, nSDRG entries, define entries, and Pinnacle logs.) These compliant datasets will then be merged with the SEND package. If the Sponsor or Sponsor's third party do not have capabilities, they should discuss conversion pricing.

Charles River Resources

Can't find what you're looking for? SEND us your questions

- Webinar | Succeeding with New SEND Requirements: Expert Panel Discussion
- Blog | SEND in the Data
- Standard Exchange of Nonclinical Data eGuide

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